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Intravenous iron therapy impact on transfusions in coronary artery bypass patients with preoperative iron deficiency anemia

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Abstract

Aim: This study aimed to investigate the effect of preoperative intravenous iron therapy on blood and blood products transfusion in patients with preoperative iron deficiency anemia and coronary artery bypass graft surgery.

Material and Methods: The records of 86 patients who underwent isolated CABG surgery at the Ankara University Faculty of Medicine Heart Center between 2019 and 2021 were retrospectively analyzed. A total of 43 patients with iron deficiency anemia who underwent preoperative IV iron therapy and those who did not undergo IV iron therapy were included in the study. Hemoglobin (Hb), ferritin, and serum iron levels were examined in the preoperative and postoperative periods.

Results: There was no difference in preoperative Hb levels, ferritin, or preoperative serum iron levels between the groups receiving IV therapy and those not receiving IV therapy ($p = 0.75$, $p = 0.06$, $p = 0.71$). There was no significant difference between the two groups in terms of early postoperative Hb and discharge Hb ($p = 0.28$; $p = 0.1$; $p > 0.05$). Hb values were found to be significantly higher in those who received IV iron therapy at the follow-up one month later (12.84±1.52 and 11.6±1.47, $p<0.001$). There was no significant relationship between the amount of erythrocyte suspension used.

Discussion: It can be said that it would be more beneficial to administer IV iron therapy and wait 3–4 weeks for patients who will undergo elective surgery with iron deficiency anemia in the pre-operative period. IV iron therapy must be applied to the patient immediately before urgent operations, such as CABG operations.

Keywords

Anemia, Iron Deficiency Anemia, Coronary Artery Bypass Graft, Patient Blood Management, Intravenous Iron Therapy

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Introduction

Anemia is a common comorbid condition in individuals who are scheduled for cardiac surgery and is found in 25–40% of patients who are scheduled for elective heart surgery [1]. Preoperative anemia in patients scheduled for cardiac surgery should be identified, evaluated, and managed in a manner aimed at minimizing transfusions of blood and blood products. According to the World Health Organization, the definition of anemia is the value at which red blood cells and their oxygen-carrying capacity are considered to be insufficient for the physiological needs of the body. These values are low hemoglobin levels below 13 g/dl for men and 12 g/dl for non-pregnant women. However, studies have suggested that 13 g/dl should be accepted as a threshold without discriminating between men and women [2]. Cardiac surgery poses a high risk of bleeding beacuse of the patient group to which it is applied, the antithrombotic drugs used, and cardiopulmonary bypass. Blood; It is a difficult, expensive, and limited resource to obtain. During the COVID-19 pandemic, there has been a drastic decrease in blood donations worldwide. "Patient blood management" (PBM) is a term used to describe an evidence-based, multidisciplinary approach to optimize the care of patients who require transfusions. The most important element in optimizing the patient's own blood is the correction of preoperative anemia [3]. Many studies have shown that 1/2–1/4 of the patients who underwent surgery were anemic, which increased the need for transfusion by 2-3 times, and the morbidity and mortality of these patients were significantly higher than those who were not preoperatively anemic. Elective surgery for an anemic patient is strictly contraindicated in PBM applications.[4] All patients included in the list should be evaluated for anemia in the patient group in which blood loss of 500 ml or more is expected during major elective surgery and/or surgery. Ideally, this examination should be performed 4-6 weeks before surgery [5]. Serum ferritin level below 30 mg/l is the most sensitive and specific test used to identify absolute iron deficiency. However, in the case of inflammation (C-reactive protein >5 mg/l) and/or transferrin saturation below 20%, a serum ferritin level below 100 mg/l indicates iron deficiency. The presence of iron deficiency, whether accompanied by anemia or not, is a condition that needs to be treated [2]. If detected 6–8 weeks before surgery, replacement therapy with oral iron preparations (high doses such as 40–60 mg/day or 80–100 mg/day) is recommended. IV iron therapy is applied in case of side effects in the gastrointestinal tract that prevent the absorption of oral iron preparations, and severe or ongoing blood loss [6]. The treatment optimizes the patient's hematopoiesis with the proper functioning of enzymatic reactions, which have an important place in cellular functions, and the increase in reticulocytes is expected to occur on the 2nd–4th days following the treatment. In this respect, intravenous iron therapy improves cellular functions even in critically ill patients who are scheduled to undergo surgery within 1-2 days, except for elective surgeries [7]. Evidence suggests that anemia is an independent risk factor for adverse outcomes such as mortality, morbidity (e.g., cardiac, respiratory, urinary tract infection, wound infections, sepsis and venous thromboembolism), length of hospital stay, and postoperative intensive care unit admission [8]. In this study, we aimed to investigate the effect of preoperative intravenous iron therapy on blood and blood products transfusion in patients who underwent coronary artery bypass graft surgery with iron deficiency anemia in the preoperative period.

Material and Methods

The study was conducted by retrospectively scanning the files of 86 patients who underwent isolated CABG surgery at the Ankara University Faculty of Medicine Heart Center between 2019 and 2021. A total of 43 patients who underwent intravenous iron therapy before surgery and those who did not receive it were included in the study. Hemoglobin, ferritin and serum iron levels of the patients were examined before and after surgery (day 1, day of discharge and one month later), and the two groups were examined in terms of transfused blood and blood products. Statistical analysis of the results was performed using the SPSS program. Patients with iron deficiency anemia (Hb < 13 gr/dL, Transferrin Saturation (TSAT) < 20%, Ferritin<100 µg/L) were included in the patients who received and did not receive 1000 mg intravenous iron (Ferric Carboxymaltose) treatment before surgery. In the study, descriptive statistics were presented with mean±standard deviation (min-max) for quantitative variables with a normal distribution, median (min-max) for variables with an abnormal distribution, and percentage for qualitative variables. When the number of groups was two, the relationship between the groups in terms of a numerical variable was examined using the "Significance Test of the Difference Between Two Means" if the parametric test assumptions were met, and the "Mann-Whitney U Test" if the parametric test assumptions were not met. The relationship between qualitative variables was evaluated using the Chi-Square Test or Fisher's Exact Test. The relationship between the two numerical variables was examined using the Spearman Correlation Coefficient. The SPSS 11.5 program was used for statistical analysis.

Ethical Approval

This study was approved by the Ethics Committee of the Sakarya University, Faculty of Medicine Non-Pharmaceutical Interventional Clinical Research (Date: 2022-01-03, No: 92660-573).

Results

The mean age of the patients (n = 43) who received 1g of IV Fe (Ferric Carboxymaltose) treatment within the scope of the study; The mean age of patients who did not receive IV Fe therapy (n=43) was 66.23±9.37; It was 67.83±8.49. The demographic characteristics were similar in the two groups. The time between intravenous iron therapy and admission to

Table 1. Preoperative Hb, preoperative ferritin and preoperative TSAT parameters of the patients

Parameters (gr/dl)	Patients receiving iron therapy (n = 43)	Patients without iron therapy (n = 43)	p
Preoperative Hb	11.54± 0.98	11.48±0.98	0.71
Preoperative Ferritin	39.28 ±28.44	38.51±29.59	0.75
Preoperative TSAT	12.20 ± 6.26	14.62±5.97	0.018

Hb: hemoglobin, TSAT: transferrin saturation

Table 2. Postoperative Early Hb, Discharge Hb, Control Hb

Parameters (gr/dl)	Patients receiving iron therapy (n = 43)	Patients without iron therapy (n = 43)	p
Postoperative early Hb	8.8± 0.79	8.6 ±0.81	0.288
Discharge Hb	10.30±1.44	9.8±1.07	0.1
Control Hb	12.84±1.52	11.6±1.47	< 0.001

Hb: Hemoglobin

the operation was calculated as 3.18± 4.9 days. In the study group, 31 (72.1%) patients who received IV Fe treatment had comorbidities, and 34 (79.1%) patients who did not receive IV Fe treatment had comorbidities. In the study group, 28 (65.1%) patients who received IV Fe treatment had diabetes mellitus, and 26 (60%) patients who did not receive IV Fe treatment had additional diabetes mellitus. In the study group, 17 (39.5%) patients who received IV Fe treatment had hypertension, and 25 (58.1%) patients who did not receive IV Fe treatment had hypertension. In the study group, 1 (2.3%) of those who received IV Fe treatment had cerebrovascular disease (CVO), and none of those who did not receive IV Fe treatment had a history of CVO. In the study group, 1 (2.3%) of those who received IV Fe treatment had malignancy, and 2 (4.7%) of those who did not receive IV Fe treatment had malignancy. In the study, the preoperative Hb value was not statistically significant between those who received IV iron therapy and those who did not receive IV iron therapy (p = 0.71). The preoperative ferritin value was not statistically significant between those who received IV iron therapy and those who did not (p = 0.75). The preoperative TSAT value was not statistically significant between those who received IV iron therapy and those who did not receive IV iron therapy (p = 0.018). The preoperative Hb,
preoperative ferritin and preoperative TSAT parameters of the patients are given in Table 1.

In the study, it was not statistically significant in terms of early postoperative Hb value between those who received IV iron therapy and those who did not receive IV iron therapy (p=0.288). The difference between the discharge Hb values between those who received IV iron therapy and those who did not was not statistically significant (p = 0.1). The control Hb (after 1 month) value was statistically significant between those who received IV iron therapy and those who did not receive IV iron therapy (p < 0.001). The postoperative early Hb, discharge Hb and control Hb parameters of the patients are given in Table 2.

In the study, the length of stay in the intensive care unit was not statistically significant between those who received iron therapy and those who did not receive iron therapy (p=0.643). The length of hospital stay was not statistically significant between those who received IV iron therapy and those who did not receive IV iron therapy (p = 0.38). The amount of erythrocyte suspension used was not statistically significant between those who received IV iron therapy and those who did not.

Discussion

The main finding of this study was that IV iron for the treatment of anemia before cardiac surgery was not associated with a lower transfusion rate compared to the control group. However, statistically significant results were obtained between control Hb values after 1 month between those who received IV iron therapy and those who did not. The number of units transfused per patient, length of intensive care unit stay, and length of hospital stay did not differ between the IV iron group and the control group. Anemia is a multifactorial disorder that can occur at any age and affects the oxygen-carrying capacity of the blood [9]. In a study conducted by Özbalcı et al. in a group of 1000 patients, iron deficiency anemia (IDA) was detected in 25% of women and 7.4% of men, while the prevalence of IDA was found to be 20.3% in all patients [10]. In our study, the rate of women with iron deficiency was found to be 61.6%. In the study conducted by Dai et al. in 10589 patients who underwent elective cardiac surgery, 2715 (26%) of them were anemic and it was shown that complications such as blood product transfusion and reoperation, prolonged ventilation, renal failure, intensive care and hospital stays, and death were significantly higher than those in non-anemic patients. Iron-deficiency anemia is the most common group of microcytic anemia. Beyond the simple hemoglobin level, the detection and treatment of preoperative iron deficiency allow doctors to predict possible risks by optimizing patient management before surgery [11]. Blood transfusion has been shown to prolong intensive care unit stays and increase the rate of organ failure. In our study, there was no significant difference in the length of stay in the intensive care unit between patients who received IV iron therapy and those who did not. The reason for this was thought to be that patients who were going to undergo CABG surgery and received intavenous iron therapy were operated on before the targeted waiting period due to urgent surgical needs. Perioperative iron therapy is recommended in surgical patients with iron deficiency anemia or suboptimal iron stores (in which the ferritin level is defined as <30µg/L) and a significant amount of blood loss is expected (sufficient blood loss to cause anemia that requires treatment). All elective surgery patients should be evaluated 4–8 weeks before surgery to manage and optimize hemoglobin and iron stores. Hemoglobin, serum ferritin, transferrin saturation, serum vitamin B12 level, and CRP levels should be checked [8, 12].

Iron is a vital element for the body, especially for metabolically active tissues such as the myocardium. Iron deficiency occurs in up to 50% of chronic heart failure (CHF) patients with both concomitant anemia and normal hemoglobin levels [13]. Patarek et al's [14] In a reperfused MI model in rats with normal iron levels, they found that intravenous administration of ferric carboxymaltose in 30 min of reperfusion did not affect post-MI mortality, left ventricular size or function, ventricular arrhythmias, the activity of mitochondrial electron transport chain enzymes, oxidative stress or inflammation marker activities, and intravenous iron therapy, although safe, was ineffective.

In contrast, a 2018 study aimed to evaluate iron status and the effect of iron supplementation in a rat model of heart failure after myocardial infarction found that heart failure alone did not cause anemia, systemic or myocardial iron deficiency, but reduced myocardial ferritin. Iron treatment increased serum Fe, ferritin, and transferrin saturation, as well as cardiac and hepatic iron content, but not myocardial ferritin, in rats with heart failure. In addition, (1) better preservation of left ventricular ejection fraction and smaller left ventricular

dilatation; (2) preserved function of Ca 2+ -handling proteins in left ventricular cardiomyocytes; and (3) decreased inflammatory marker CRP was detected.They revealed that it prevented the degradation of handling proteins and reduced the level of the inflammatory marker CRP. These results suggest that iron abnormalities in heart failure can be very complex and that further studies are certainly needed to find more appropriate and sensitive biomarkers of iron status in hearts that develop insufficiency not only at the systemic but also at the tissue, cellular and subcellular levels [15]. In a study by Gunaydın et al., which examined approximately 92,000 patients who applied to the cardiovascular surgery outpatient clinic for 2 years, preoperative iron deficiency anemia was detected in 40% of the patients. Within the scope of preoperative anemia treatment, which is the most important component of HCI, iron was used as one dose (1000 mg) at the first hospitalization and one dose the day before surgery in 495 coronary bypass surgery patients without the chance to postpone surgery for a long time, without transfusion in 306 patients, and <1 dose in 124 patients. They demonstrated that it significantly reduces the need for transfusion. [16]. Intravenous iron should be used as the first line of treatment in patients who do not respond to oral iron or who are intolerant, or if surgery is scheduled within 6 weeks of the diagnosis of iron deficiency. After intravenous Fe treatment, hemoglobin response starts immediately: 50% on the 5th day, 75% on the 10–14th day, and a maximum increase within 3 weeks [17]. Recently, Hong-Mei et al. found that in a systematic review-meta-analysis of 1350 patients, IV iron therapy at doses of 200 mg–1000 mg before surgery at different times between 1 day and 10 weeks did not make a difference in the number of transfusion units, intensive care unit stay, and hospital stay, similar to our study, but provided a significant result on mortality [18]. In our study, hemoglobin values were found to be significantly higher in those who received intravenous iron therapy when hemoglobin values were examined in the first month of follow-up between both groups. In patients with iron deficiency anemia who needed urgent intervention such as CABG operation, IV iron therapy applied just before the operation was thought to provide a significant increase in hemoglobin values at the end of the fourth week.

Conclusion

In conclusion, it can be said that administering IV iron therapy to patients who will undergo elective surgery with iron deficiency anemia in the pre-operative period and waiting 3–4 weeks will produce better results. It should not be ignored that in urgent cases such as CABG operations, which do not have a chance to wait, IV iron therapy applied before the operation also provides a significant increase in Hb levels when the 1-month results are examined. It is thought that it will be better to perform the examinations of patients with a high risk of bleeding and who will undergo major surgical operations 4-6 weeks in advance and to wait 6–8 weeks before performing appropriate iron therapy in patients with anemia. In addition, it has been determined that IV iron therapy must be applied to the patient just before the urgent operations, except for elective surgeries such as CABG operations, and effective results can be obtained in the evaluations made 1 month after the application.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or compareable ethical standards.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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